REMARKS/ARGUMENTS

In this Amendment, claims 45-61, 63-67, 69-78, 80, 81, 87-93, 96, 99-122, 125, 128-135, 137, 139-143 and 146-150 are currently amended and claims 1-44, 62, 68, 79, 82-86, 94, 95, 97, 98, 123, 124, 126, 127, 136 and 138 are canceled without prejudice or disclaimer. Claims 144 and 145 were previously presented and claims 151-160 are newly added. No new matter has been introduced into the application by virtue of the amended and new claims. A number of the currently amended claims contain formalistic changes to the claim language.

Support for the amended and new claims is found throughout the specification of the instant application and in the prior claims. Specifically, amended claim 45 is supported by prior claims 79, 82-86, 94, 95, 97, 98 and in the instant specification on page 11, fourth paragraph. Amended claim 56 is supported by prior claims 62, 68, 123, 124, 126 and 127. Additional support for the amended and new claims is found, for example, in the instant specification, *inter alia*, on page 20, third and fourth paragraphs, on page 21, first full paragraph, on pages 23-24, Table II and on pages 26-27, Example 4.

Accordingly, claims 45-61, 63-67, 69-78, 81, 87-93, 96, 99-122, 125, 128-135, 137 and 139-160 are currently pending in the application.

Applicants acknowledge that the Examiner objected to prior claims 62, 68, 86-88, 94-99 and 123-128 as being dependent upon a rejected base claim and stated that these claims would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. (page 3 of the 07/12/2004 Office Action). Applicants submit that the presently amended claims address the Examiner's objections to the afore-listed claims such that the presently pending claims are allowable.

In addition, Applicants acknowledge that claims 137-150 have been deemed allowable by the Examiner. (page 3 of the 07/12/2004 Office Action).

Applicants respectfully submit that the rejections in the 07/12/2004 Office Action have been addressed herein as if they had been asserted against the presently amended and new claims.

The claims fulfill the requirement of 35 U.S.C. §103(a)

Claims 45-61, 63-67, 69-85, 89-93, 100-123 and 129-136 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over European Patent Application No. 770 387 (hereinafter "EPA '387").

The Examiner characterizes EPA '387 as teaching "a composition comprising 0.1-2% central acting anesthetic, 5-30% long chain and/or medium chain triglycerides, and 0.5-2% emulsifier". The Examiner further states that olive oil is disclosed; lecithin is specified; a ratio of 10:-1:10 long to medium chain triglycerides is specified; mannitol is disclosed as a tonicity agent; a droplet size of 0.2-0.35 μm is specified; and long term stable emulsions are disclosed in EPA '387. According to the Examiner, "it would have been obvious to one of ordinary skill in the art to deliver propofol, well-known in the art as a central acting anesthetic, in the vehicle of EPA '387 to achieve the effect of long term stability."

Applicants respectfully contend that the presently claimed invention, considered as a whole, is not made obvious by the teaching and disclosure of EPA '387.

It is submitted that the presently claimed invention must be considered as a whole in determining differences between the prior art and the presently claimed invention. M.P.E.P. §2141.02. Considered in its entirety, the presently claimed invention provides compositions having components, combinations of components, and/or amounts of components that are not taught or suggested in EPA '387. Further, all claim limitations must be taught or suggested by the cited art reference. M.P.E.P. §2143.03. In the instant case, EPA '387 states that its contemplated composition in the form of an oil-in-water emulsion consists essentially of "5 to 30% (w/v) of an oily carrier consisting of long-chain triglycerides (LCT) and/or medium-chain triglycerides (MCT), as well as 0.5 to 2% (w/v) of an emulsifier, 0.1 to 2% (w/v) of a local

anesthetic or a centrally-acting analgesic and conventional additives. (Col. 3, [0017] and Examples 1-4). Moreover, the compositions according to EPA '387 do not contain nonionic surfactants.

Applicants' presently claimed compositions are distinct from those taught or suggested in EPA '387, considered in its entirety. Applicants' compositions differ from those taught in EPA '387 in that Applicants' compositions inhibit microbial growth and prevent irritation using lower amounts of ingredients, for example, propofol-soluble diluent in an amount of less than about 5%. This is distinctly different from what is taught and disclosed in EPA '387. Further, Applicants' compositions do not exclude nonionic surfactants, in contrast to what is affirmatively taught in EPA '387. Instead, Applicants' compositions can contain both charged and uncharged phospholipids. (*See, e.g.,* the instant specification on page 10, lines 9-10).

EPA '387 is silent regarding the viscosity of its described compositions; however, in view of the differences in the combinations and amounts of ingredients comprising Applicants' presently claimed compositions and the compositions disclosed in EPA '387, it is likely that the viscosity is not the same. Applicants teach that the viscosity of the claimed propofol-containing compositions is surprisingly high. *See, e.g.,* the instant specification on page 11, fourth paragraph on the page and on page 21, first full paragraph on the page.

Contrary to the Examiner's statement that no criticality has been shown for the mannitol concentration, it is respectfully submitted that Applicants teach that propofol formulations according to the instant invention made with polyhydroxy compounds as taught by Applicants provide compositions of relatively high viscosity. *See, e.g.,* the instant specification on page 11, fourth paragraph from the top of the page. As taught by Applicants, the high viscosity may contribute to the advantages of Applicants' compositions, such as a decrease in hemolytic potential upon use.

Applicants also surprisingly found and teach in the instant disclosure that simply by increasing the amount of oil in a propofol formulation did not result in a less irritating formulation. (*See, e.g.,* the instant specification on page 20, Example 2, third paragraph on page.). Applicants' unexpected findings led to their discovery of new compositions containing

lower levels of oil to achieve and provide several advantages to the art, namely, less tissue irritation at a site of injection, a lower level of hemolysis and an inhibition of microbial growth.

However, as taught by Applicants, the advantages afforded by Applicants' new compositions do not result from merely lowering the amount of oil in the compositions, but can be attributed to a combination of cooperative effects among the ingredients which leads to less irritating and more stable formulations that are not contaminated by microorganisms. *See,* the instant specification on page 21, second full paragraph on the page, Examples 1 and 2, and Table II.

Applicants also provide to the art stable, high potency compositions containing the above-mentioned combinations of ingredients, as well as high concentrations of propofol, e.g., in amounts of about 10% to 15%. (*See, e.g.,* Example 4, pages 26 and 27 of the instant specification.). Such high potency formulations of propofol allow for a lower volume of a formulation to be administered intravenously, while delivering the same effective dose of drug. (*See, e.g.,* page 27, fourth paragraph, of the instant specification.).

It is thus respectfully submitted that there is no teaching or suggestion in EPA '387 that would lead one having skill in the art to make the modifications that would be necessary to achieve Applicants' presently claimed invention with a reasonable expectation of success. There is no teaching or suggestion in EPA '387 to use lower amounts of LCT or MCT than are disclosed in this reference, and/or to use high amounts of drug with lower amounts of oily carrier, in combination. Further, EPA '387 neither teaches nor recognizes viscosity as being a critical parameter of its disclosed compositions.

Accordingly, in view of the foregoing, it is respectfully submitted that the presently claimed invention is not obvious over the cited EPA '387 reference. Withdrawal of the rejection under 35 U.S.C. §103(a) is thus respectfully requested.

CONCLUSION

Applicants respectfully submit that this application is now in condition for allowance. An action progressing this application to issue is courteously urged.

Should any additional fees be deemed to be properly assessable in this application for the timely consideration of this amendment and response, or during the pendancy of this application, the Commissioner is hereby authorized to charge any such additional fee(s), or to credit any overpayment, to Deposit Account No. **50-0311**, Reference No. **28069-504**, Customer No. **34537**.

If the Examiner is of the opinion that further discussion of the application would be helpful, the Examiner is hereby respectfully requested to telephone the undersigned at (212) 692-6742 and is assured of full cooperation in an effort to advance the prosecution of the instant application and claims to allowance.

Respectfully submitted,

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